

### ***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 1, 3, 5-10, 13, 16, 17, 19, 26, 28, 29, 34-38 and 40-44 are pending in the application, with claims 1, 37 and 38 being the independent claims. Claims 1 and 37 were amended as discussed with the Examiner during the Examiner interview of March 8, 2004. Claims 1, 7, 10 and 37 were amended to maintain the convention of using hyphens rather than arrows in the claim language. Support for the amendment can be found, *inter alia*, at page 18, lines 26-29 and page 19, lines 11-15. Claim 40 was amended to correct a typographical error. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding rejections and that they be withdrawn.

### ***Examiner Interview***

Applicant's undersigned representative thanks the Examiner for the courteous and helpful telephonic interview conducted on March 8, 2004.

### ***Substance of the Interview***

In the Examiner Interview of March 8, 2004, the outstanding rejection of claims 1, 3, 5-10, 13, 16, 17, 19, 26, 28, 29, 34-37 under 35 U.S.C. § 112, second paragraph, was discussed. In view of the recitation of the term "frame shift mutation," the Examiner was

reluctant to allow the claims, arguing that the term "frame shift mutation" was indefinite because frame shift mutants would result in the loss of polymerase activity. Applicant's representative pointed out that the claimed polymerases have polymerase activity, and identified several types of frame shift mutations that would not affect polymerase activity. The Examiner admitted that the claimed polymerases have polymerase activity and acknowledged that the types of frameshift mutants identified by Applicant's representative would have polymerase activity, yet still was reluctant to allow the claims with the term "frame shift mutation."

The outstanding rejection of claims 1, 3, 5-8, 10, 13, 16, 17, 19, 26, 28, 29, and 34-37 under 35 U.S.C. § 112, first paragraph, was also discussed. Applicant's representative argued that the written description requirement of § 112 is met because the specification provides a representative number of mutant polymerases in accordance with the invention, and assays to construct and isolate such mutants. The Examiner indicated that he would favorably consider such arguments in a formal written response.

#### ***Information Disclosure Statement***

Applicant thanks the Examiner for considering document AI1 cited in the Second Supplemental Information Disclosure Statement filed on November 21, 2001 and documents AN2 and AT15 cited in the Fifth Supplemental Information Disclosure Statement filed on October 9, 2003, and providing an initialed copy of the corresponding 1449 forms.

***Rejections under 35 U.S.C. § 112, second paragraph***

The withdrawal of the rejection of claims 1, 3, 5-10, 13, 16, 17, 19, 26, 28, 29, and 34-37 under 35 U.S.C. § 112, second paragraph, as being indefinite with respect to the metes and bounds of the 3'-5' and 5'-3' exonuclease domains is acknowledged and appreciated by Applicant. (Paper No. 34, at page 2.)

The Examiner maintained the rejection of claims 1, 3, 5-10, 13, 16, 17, 19, 26, 28, 29, and 34-37 as being indefinite in that the recitation "wherein said mutation is selected from the group consisting of: a deletion, a single or double substitution, a frame shift mutation and an insertion" is unclear. (Paper No. 34, at page 2.) According to the Examiner,

the inclusion of frame shift mutations in the group of sought mutations is unclear as frame shift mutations would result in the [sic] not only the potential loss of 5'-3' exonuclease activity, 3'-5' exonuclease activity and discriminatory behavior against dideoxynucleotides, but the loss in polymerase activity itself . . . . Thus a frameshift mutation in any of the 3'-5' exonuclease domain, the 5'-3' exonuclease domain or the O-helix domain would by definition effect the polymerase domain.

*Id.* Applicant respectfully disagrees.

As Applicant's representative discussed during the Examiner interview, a frame shift mutation would not necessarily lead to any loss of activity of the claimed DNA polymerases. Claim 1, for example, is directed to a *Thermotoga maritima* DNA polymerase which is modified in "at least two ways." Therefore, a first frame shift mutation that alters the translation coding frame (by other than a multiple of three base pairs), followed by a second frame shift mutation that reverts the translation coding frame back to the original coding

frame would not necessarily affect the polymerase domain / activity. Consequently, Applicant submits that the meaning of "frame shift mutation" would be clear to those skilled in the art, and certainly is not indefinite under § 112.

However, in an effort to advance prosecution, Applicant has amended claims 1 and 37 to remove the recitation of the term "frame shift mutation." During the Examiner interview, the Examiner indicated that such an amendment would be favorably considered.

***Rejections under 35 U.S.C. § 112, first paragraph***

The Examiner maintained the rejection of claims 1, 3, 5-8, 10, 13, 16, 17, 19; 26, 28, 29 and 34-37 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. (Paper No. 34, at page 2.) The Examiner alleged that "the specification does not disclose a representative number of species of the claimed genus which includes an **infinite number of amino acid variants** of any *Tma* DNA polymerases." (Paper No. 32, at page 10, emphasis in original; rejection maintained in Paper No. 34, at page 2.)

Applicant respectfully disagrees with the Examiner's reasoning. The Court of Appeals for the Federal Circuit ("Federal Circuit") has provided substantial guidance regarding the written description requirement of 35 U.S.C. § 112 and satisfaction of the "possession test." In particular, the Federal Circuit has instructed that a specification that teaches one of skill in the art to make and use an invention can be sufficient to show a person of ordinary skill in the art that the inventor possessed the invention. *See Moba, B.V.* 249697-1

*v. Diamond Automation, Inc.*, 325 F.3d 1306, 1321 (Fed. Cir. 2003) ("the specification that taught one of skill in the art to make and use an invention also convinced that artisan that the inventor possessed the invention.").

The point of the written description requirement is to ensure that the Applicant possessed, at the time of filing, what is now being claimed. In other words, the originally-filed disclosure should convey to one of skill in the art that the Applicant had possession of the concept of what is claimed. *See Ex parte Parks*, 30 USPQ2d 1234 (BPAI 1994). In view of the extensive "make and use" teachings in Applicant's specification, persons skilled in the art certainly would recognize that Applicant had possession of the claimed polymerases. Hence, the present specification clearly and completely meets the written description requirements under 35 U.S.C. § 112, first paragraph. Rather than reiterate Applicant's previous arguments along these lines, Applicant refers the Examiner to the responses filed on, *inter alia*, May 21, 2001, December 18, 2001, January 8, 2003, and October 9, 2003.

During the Examiner interview, Applicant's representative reminded the Examiner that an applicant is not required to disclose or provide a working example of every species of a given genus in order to meet the written description requirement of 35 U.S.C. § 112. *See Regents of Univ. of Calif. v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997). Rather, a description of a genus may be achieved by a recitation of a representative number of embodiments falling within the scope of the genus. *Id.* at 1569. Applicant's representative argued that the present specification describes a sufficient number of representative examples of the claimed genus. For example, the specification discloses that the 5'-3' exonuclease activity can be reduced or eliminated by mutating the DNA polymerase gene by

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a variety of mutations at any one of six conserved amino acids that are associated, including Asp<sup>8</sup>, Glu<sup>112</sup>, Asp<sup>114</sup>, Asp<sup>115</sup>, Asp<sup>137</sup> and Asp<sup>139</sup>, among others. *See* specification at page 19, lines 11-25. Applicant's representative noted the specification also provides detailed experimental methods to construct, identify and assay mutant polymerases within the scope of the claims. *See* Example 16 of the specification, at page 49. Applicant's representative also submitted that the 3'-5' exonuclease domain and the 5'-3' exonuclease domain of *Tma* DNA polymerase are well-characterized in the art. *See* Gelfand *et al.*, U.S. Patent No. 5,374,533. Taken together, these disclosures provide numerous representative examples of the claimed genus, and detailed description for the construction and characterization of other mutant polymerases within the scope of the claims. Under the standard of *Eli Lilly*, Applicant's specification therefore provides a representative number of embodiments to indicate possession of the claimed invention.

Finally, Applicant points out that even though the claims recite an insertion and deletion mutation, the resultant polypeptide must still have a molecular weight of about 100 kilodaltons. This limitation provides additional structural information regarding the size of the resultant *Tma* DNA polymerase mutants. Thus, the claimed genus would not include an "infinite number of amino acid variants."

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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